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EXAMINER	
CANELLA, KAREN A	
ART UNIT	**PAPER NUMBER**
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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/676,340	Applicant(s) SUBJECK ET AL.	
	Examiner Karen A Canella	Art Unit 1642	

-- The MAILING DATE of this communication appears on th cov r sh et with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-10,16-23,33,34 and 46-69* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-10,16-23,33,34 and 46-69* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Please note that the examiner assigned to this application has changed.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 8, 2003 has been entered.

Claims 1, 7, 9, 21, 46-51, 55-57 and 56 have been amended. Claims 1-10, 16-23, 33, 34, 46-69 are pending and under consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Claims 1-6, 16, 17, 33, 58, 59, 60 , 61 and 63 are rejected under 35 U.S.C. 102(b) as being anticipated by Mizzen et al (WO 98/23735). Claim 1 is drawn to a pharmaceutical vaccine composition comprising an isolated stress protein complex and a physiological acceptable carrier, wherein the stress protein complex comprises an hsp110 polypeptide and an immunogenic polypeptide. Claim 2 embodies the pharmaceutical composition of claim 1 wherein the hsp110 polypeptide is complexed with the immunogenic polypeptide. Claim 3 embodies the pharmaceutical composition of claim 2, wherein the hsp110 polypeptide is complexed with the immunogenic polypeptide by non covalent interaction. Claim 4 embodies the pharmaceutical composition of claim 2, wherein the complex comprises a fusion protein. Claim 5 embodies the pharmaceutical composition of claim 1, wherein the complex is derived from a tumor. Claim 6 embodies the pharmaceutical composition of claim 1, wherein the complex is derived from a cell infected with an infectious agent. Claim 16 embodies the pharmaceutical composition of claim 1, wherein the immunogenic polypeptide comprises a cancer antigen. Claim 17 embodies the pharmaceutical composition of claim 16, wherein the immunogenic polypeptide comprises a her 2/neu peptide.

Claim 33 is drawn to a method for inhibiting tumor growth in a subject comprising administering to said subject an effective amount of the pharmaceutical composition of clam 16 to elicit an anti-tumor immune response in the subject, and thereby inhibiting tumor growth in the subject. Claim 58 embodies the method of claim 33 wherein the hsp110 polypeptide is complexed with the immunogenic polypeptide. Claim 59 embodies the method of claim 33 wherein the hsp110 polypeptide is complexed with the immunogenic polypeptide by non-covalent interaction. Claim 60 embodies the method of claim 33 wherein the complex of the pharmaceutical composition comprises a fusion protein. Claim 61 embodies the method of claim 31 wherein the complex of the pharmaceutical composition is derived from a tumor. Claim 63 embodies the method of claim 33 wherein the immunogenic polypeptide of the pharmaceutical composition comprises a her2/neu peptide.

Mizzen et al disclose a vaccine for inducing cell-mediated immunity comprising one or more stress proteins and one or more antigens (page 10, lines 9-23), wherein the preferred antigens are tumor associated antigens (page 6, lines 12-24) and that useful tumor associated antigens are her2/neu (page 14, lines 16-18) and influenza antigens (page 5, line 5 to page 6, line 8). Mizzen et al contemplates that the vaccines comprise mixtures of antigens and stress protein, conjugates of antigens and stress proteins and fusion proteins comprising antigens and stress proteins (page 12, lines 2-20). Mizzen et al disclose the stress protein of Hsp110 as an example of the stress proteins of the invention (page 23, lines 6-10). Mizzen et al disclose the pharmaceutically acceptable carrier of 2mM sodium phosphate and 150mM NaCl at pH 7 (page 41, lines 4-7). Mizzen et al generally teach that the vaccines comprising stress proteins and an antigen are useful in the treatment of a bacterial pathogen in a mammal (page 12, lines 29-32), thus fulfilling the specific embodiments of claim 6.

Applicant argues that Mizzen et al do not teach the therapeutic properties of hsp110, and that although hsp110 is mentioned as an example of a heat shock protein, no basis for expecting the structural dissimilar hsp110 to have the same immunogenic utility as hsp70 is provided by Mizzen et al. Applicant contends that because one of skill in the art would not have had a reasonable expectation of success with a pharmaceutical composition comprising hsp110 complexed with an immunogenic polypeptide in the absence of data demonstrating the ability to

elicit an effective immune response, none of the cited references provides an enabling disclosure or suffices to place the public in possession of the invention. This has been carefully considered but not found persuasive. The general teachings of Mizzen et al are a composition comprising a stress protein and an antigen against which an immune response is desired (page 12, lines 2-4). On page 18, lines 32-34, Mizzen et al teach that "Any suitable stress protein (heat shock protein (hsp) can be used in the compositions of the present invention". Mizzen et al provide working examples of immunogenic compositions comprising hsp70 (examples 2 and 3, pp. 36-39), hsp71 (pp. 40-42)-, and hsp65 (example 4, pp. 42-46) and hsp71 (example 5, pp. 46-48). Mizzen et al do no provide working examples with Hsp110 as noted by applicant, however, on page 22, lines 16-24, Mizzen et al state "Stress genes and proteins for use in the present invention are those well known in the art and include, for example, Hsp100-200, Hsp100, Hsp90, Lon, Hsp70, Hsp60, Tf55, Hsp40, FKBPs, cyclophilins, Hsp20-30, ClpP, GrpE, Hsp10, ubiquitin, calnexin and protein disulfide isomerases". Mizzen et al teach the group of stress proteins comprising Hsp100 -Hsp110 (page 23, lines 10-14). One of skill in the art would conclude without a doubt that Mizzen et al is specifically teaching that Hsp110 has the properties of a stress protein that are consistent with the composition of Mizzen et al comprising a stress protein and an immunogenic polypeptide. Applicant argues that the mere fact that hsp110 has been identified as a stress protein is not enough to indicate that it could be used to inhibit cancer or other diseases. This has been considered but not found persuasive. Mizzen et al do more than identify hsp110 as a stress protein, because Mizzen et al teach Hsp110 as part of the composition comprising the immunogenic polypeptide.

Claims 1-8, 16, 17, 33, 58-63 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mizzen et al (WO 98/23735) in view of the abstract of Wang et al (FEBS Letters, 1999 February, Vol. 464, pp. 98-102) . The specific embodiments of claims 1-6, 16, 17, 33, 58, 59, 60 , 61 and 63 are set forth above. Claim 7 embodies the pharmaceutical composition of claim 1, wherein the stress protein complex further comprises a polypeptide selected from the group consisting of hsp70, hsp90, grp78 and grp94. Claim 8 embodies the pharmaceutical composition of claim 1, wherein the stress protein complex comprises hsp110 complexed with hsp70 and hsp25. Claim 62 embodies the method of claim 33 wherein the hsp110 is complexed with hsp70 and hso25.

Mizzen et al teach the specific embodiments of claims 1-6, 16, 17, 33, 58, 59, 60 , 61 and 63 for the reasons set forth in the section above. Mizzen et al generally teach that the vaccines comprising stress proteins and an antigen are useful in the treatment of a bacterial pathogen in a mammal (page 12, lines 29-32) and that the stress proteins of Hsp70 and Hsp20-30 are among the major determinants recognized in the immune response to infection by M. tuberculosis (page 21, lines 18-22). Mizzen et al do not specifically teach a vaccine composition comprising hsp110 complexed to hsp70 and hsp25.

The abstract of Wang et al teach that native Hsp110 forms a complex with Hsp25 and Hsp70 (lines 7-9).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to use a pharmaceutical composition comprising a complex of hsp110, hsp25 and hsp70 proteins as a vaccine for M tuberculosis. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Mizzen et al on (a) pharmaceutical compositions comprising heat shock proteins such as Hsp110 for the treatment of a bacterial pathogens and (b) the immunogenicity of the Hsp25 and Hsp70 proteins produced by an M tuberculosis infection, and the teachings of Wang et al on the native interaction of the Hsp110, Hsp25 and Hsp70 proteins. One of skill in the art would recognize that the heat shock proteins of Hsp25 and Hsp70 proteins are antigens produced by the intracellular M tuberculosis pathogen, and would be therefore motivated in using said proteins in a vaccine against tuberculosis.

Applicant argues that none of the above references teaches a composition comprising hsp110 as an immunogen because it was not known that hsp100 was immunogenic or otherwise useful in the inhibition of cancer or infectious disease. This has been considered but not found persuasive, for the reasons set forth above, that Mizzen et al specifically teaches Hsp110 as an embodiment of the composition comprising the stress protein and the immunogenic polypeptide. Further Mizzen et al teach that the stress proteins hsp20-30 are immunogenic proteins recognized in the immune response against M tuberculosis. Mizzen et al do not specifically teach Hsp25 as a specific embodiment of the Hsp20-30 proteins, but it is recognized in the art that the Hsp20-30 proteins are the "small" heat shock proteins, and Hsp25 is a member of the "small" heat shock

proteins. Further, the abstract of Wang et al teach that Hsp110, Hsp25 and Hsp70 form a complex. Thus, it would be obvious to include the heat shock proteins of Hsp25and Hsp70 in a composition with Hsp110 because the Hsp70 protein is an immunogenic protein that evokes an immune response to a M tuberculosis infection, in addition to the hsp20-30, small heat shock proteins. Additionally, it would be obvious to combine Hsp110 with Hsp70 and Hsp25 because Wang et al teach that Hsp110, Hsp25 and Hsp70 complex together.

Claims 1-6, 16, 17, 22, 33, 58, 59, 60 , 61, 63 and 68 are rejected under under 35 U.S.C. 103(a) as being unpatentable over Mizzen et al (WO 98/23735) in view of Wallen et al (6,066,716). The specific embodiments of claims 1-6, 16, 17, 33, 58, 59, 60 , 61 and 63 are set forth in section 8 above. above. Claim 22 is drawn to the pharmaceutical composition of claim 1, wherein the complex has been heated so as to enhance binding of the hsp110 polypeptide to the immunogenic polypeptide. Claim 68 embodies the method of claim 33 wherein the complex of the pharmaceutical composition is heated so as to enhance the binding of the hsp110 polypeptide to the immnogenic polypeptide.

Mizzen et al teach the specific limitations of claims 1-6, 16, 17, 33, 58, 59, 60 , 61 and 63 for the reasons set forth above. Mizzen et al do not teach the heating of the complex.

Wallen et al teach a method for the purifying heat shock proteins in native association with peptide inside the cell (column 3, lines 25-31). Wallen specifically teaches that members of the hsp104-105 family are particularly useful (column 3, lines 52-57) and identifies hsp110 as a member of the aforesaid family (column 4, lines 3-4). Wallen et al teach that incubation between 37 degrees and 50 degrees increases the number of heat shock proteins (column 3, lines 5-7).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to heat a cellular lysate comprising the hsp110 protein and the immunogenic polypeptide.

One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Wallen et al on the increase in the level of heat shock proteins upon heating of a cellular lysate. It is reasonable to assume the increased level of heat shock proteins would result in a concomitant increase in the number of heat shock proteins

complexed to immunogen because Wallen et al teach that heat shock proteins are associated with peptides inside the cell.

Applicant argues that Wallen describes a method for purifying heat shock proteins complexes which comprises the steps of adding a solution containing heat shock complexes in which heat shock proteins are associated with peptides, polypeptides, denature proteins complexes in which to a column containing ADP matrix to bind the heat shock proteins. Applicant contends that Wallen et al teach away from the instant invention in that hsp110 does not bind to ATP or ADP. This has been considered but not found persuasive. Applicant sites figure 4 of Oh et al in support of the allegation that hsp110 does not bind to ATP. On examination of the legend for figure 4B it is indicated in the last two lines that the column marked "Beads" is proteins remaining on the ATP agarose after ATP elution. Clearly the hsp110 protein is bound to the ATP agarose and exposure to ATP solution competes with the ATP of the agarose for binding of the hsp110 indicated by the decrease in the amount of material on the ATP agarose after the ATP elution.

Claims 1-6, 16, 17, 23, 33, 58, 59, 60 , 61, 63 and 69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mizzen et al (WO 98/23735) in view of Srivastava et al (WO 95/24923) and either of Dong et al (Pharmaceutical Biotechnology, 1995, Vol. 6, pp. 625-643) or Heath, Pharmaceutical Biotechnology, 1995, Vol. 6, pp. 645-658). The specific embodiments of claims 1-6, 16, 17, 33, 58, 59, 60 , 61 and 63 are set forth above. Claim 23 embodies the pharmaceutical composition of claim 1, further comprising an adjuvant. Claim 69 embodies the method of claim 33 wherein the pharmaceutical composition further comprises an adjuvant. Mizzen et al teach the specific limitations of claims 1-6, 16, 17, 33, 58, 59, 60 , 61 and 63 for the reasons set forth above. Mizzen et al do not teach a pharmaceutical composition comprising hsp110 in combination with an adjuvant.

Srivastava et al teach vaccines comprising stress protein-peptide complexes and cytokines (abstract and page 48, lines 16-21). Either of Dong et al or Heath et al identify cytokines as immunological adjutants.

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to administer the vaccine taught by Mizzen et al with a cytokine as an adjuvant.

One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teaching of either Dong et al or Heath on the efficacy of cytokines as immunological adjutants and the teachings of Srivastava et al on the combination of stress-protein-peptide vaccines with cytokines for the initiation of cytotoxic T-cell response against said peptide.

Applicant does not specifically argue against this combination of references, however, applicant argues that Mizzen et al do not teach a composition comprising hsp110 as an immunogen because it was not known that hsp100 was immunogenic or otherwise useful in the inhibition of cancer or infectious disease. This has been considered but not found persuasive, for the reasons set forth above, that Mizzen et al specifically teaches Hsp110 as an embodiment of the composition comprising the stress protein and the immunogenic polypeptide.

Claims 1-6, 16-18, 33, 58, 59, 60 , 61, 63 and 64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mizzen et al (WO 98/23735) in view of Cheever et al ((U.S. 5,726,023). The specific embodiments of claims 1-6, 16, 17, 33, 58, 59, 60, 61 and 63 are set forth above. Claim 18 embodies the pharmaceutical composition of claim 17, wherein the her 2/neu peptide is derived from the intracellular domain of her 2/neu. Claim 21 embodies the composition of claim 16 wherein the cancer antigen is a colon cancer antigen.. Claim 64 embodies the method of claim 63 wherein the her2/neu peptide is derived form the intracellular domain of her2/neu. Mizzen et al disclose a vaccine for inducing cell-mediated immunity comprising one or more stress proteins and one or more antigens (page 10, lines 9-23), wherein the preferred antigens are tumor associated antigens (page 6, lines 12-24) and that useful tumor associated antigens are her2/neu (page 14, lines 16-18). Mizzen et al do not specifically teach the intracellular domain of said protein.

Cheever et al teach that rats immunized with the intracellular domain (ICD) of Her2 developed higher levels of Neu peptide specific T-cell responses as well as Neu protein specific

T-cell responses in contrast to rats immunized with the extracellular domain (ECD) of Her2 (column 30, line 47 to column 32, line 8). Cheever et al teach that the expression of Her-2/neu is associated with colon cancer (claim 2).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to use the ICD as the tumor-associated antigen in the vaccine taught by Mizzen et al.

One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Cheever et al on the advantages of eliciting an immune response against the ICD of Her2/neu versus the ECD of Her2/neu.

Applicant does not specifically argue against this combination of references, however, applicant argues that Mizzen et al do not teach a composition comprising hsp110 as an immunogen because it was not known that hsp100 was immunogenic or otherwise useful in the inhibition of cancer or infectious disease. This has been considered but not found persuasive, for the reasons set forth above, that Mizzen et al specifically teaches Hsp110 as an embodiment of the composition comprising the stress protein and the immunogenic polypeptide.

Claims 1-6, 16-18, 20, 21, 33, 58, 59, 60 , 61, 63 and 64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mizzen et al (WO 98/23735) and Cheever et al ((U.S. 5,726,023) as applied to claims 1-6, 16-18, 33, 58, 59, 60 , 61, 63 and 64 above, and further in view of Eberlein et al (U.S. 5,550,214). The specific embodiments of claims 1-6, 16, 17, 33, 58, 59, 60, 61 and 63 and the teachings of Mizzen and Cheever which render these claims obvious is set forth above. Claim 20 embodies the pharmaceutical composition of claim 17 wherein the her-2/neu peptide is derived from the transmembrane region of her-2/neu Cheever et al teaches compositions comprising either the transmembrane domain or the extracellular domain of her-2/nei. Neither Mizzen et al nor Cheever et al teach a composition comprising the transmembrane region of Her-2/neu.

Eberlein et al teach immunogenic peptides derived from Her-2/neu and the presentation of said peptides by HLA-A2 molecules leading to recognition by cytotoxic T-lymphocytes. This invention is based, in part, on our discovery that HER2/neu antigenic peptides described herein,

when presented by HLA-A2 molecules, are recognized by cancer-specific cytotoxic T lymphocytes from many different tumors.. Eberlein et al specifically teach that at least one of these peptides derived from a fragment of the HER2/neu oncogene protein involves a point mutation found in the transmembrane portion of the tumor-derived HER2/neu protein and is not expressed in normal tissue (column 6, lines 6-17).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to substitute the peptide derived from the transmembrane region of Her-2/neu for the intracellular portion of the Her-2/neu protein.

One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Eberlein on the immunogencity of peptides derived from fragments comprising a point mutation consistent with oncogenic transformation. One of skill in the art would be motivated to induce a immune response against said transmembrane fragment in order to target transformed cells.

Applicant summarizes the arguments stating that the references actually teach away from the instant invention because the teachings of the prior art regarding hsp90, hsp70, hsp60, hsp20-30 and ubiquitin would lead the skilled artisan away from the use of hsp110. This has been considered but not found persuasive. The demonstration of success with other heat shock proteins would not lead one of skill in the art away from the use of hsp110 as a stress protein in combination with an immunogenic polypeptide because Mizzen et al teach that Hsp110 is a stress protein which is part of the disclosed composition. Further, the courts have determined that disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. In re Susi, 440 F.2d 442, 169 USPQ 423 (CCPA 1971). and In re Gurley, 27 F.3d 551, 554, 31 USPQ2d 1130, 1132 (Fed. Cir. 1994) (The invention was directed to an epoxy impregnated fiber reinforced printed circuit material. The applied prior art reference taught a printed circuit material similar to that of the claims but impregnated with polyester imide resin instead of epoxy. The reference, however, disclosed that epoxy was known for this use, but that epoxy impregnated circuit boards have "relatively acceptable dimensional stability" and "some degree of flexibility," but are inferior to circuit boards impregnated with polyester imide resins. The court upheld the rejection concluding that

applicant's argument that the reference teaches away from using epoxy was insufficient to overcome the rejection since "Gurley asserted no discovery beyond what was known in the art." 27 F.3d at 554, 31 USPQ2d at 1132. In the instant case, Mizzen et al does not provide any disclosure that the use of hsp110 in place of the hsp used by Mizzen in at in the examples would not be as effective in the composition comprising the stress protein and the immunogenic polypeptide. Thus, the working examples of compositions comprising other heat shock proteins than the instant hsp110 cannot be considered as teaching away from the compositions comprising hsp110.

Claims 1-6, 16, 17, 19, 33, 58, 59, 60 , 61 and 63 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mizzen et al (WO 98/23735) in view of Hudziak et al (U.S. 6,015,567).

The specific embodiments of claims 1-6, 16, 17, 33, 58, 59, 60 , 61 and 63 are set forth above. Claim 19 embodies the pharmaceutical composition of claim 17, wherein the her 2/neu peptide is derived from the extracellular domain of her 2/neu. Claim 65 embodies the method of claim 33 wherein the her2/neu peptide is derived from the extracellular domain of her2/neu. Mizzen et al disclose a vaccine for inducing cell-mediated immunity comprising one or more stress proteins including hsp110 and one or more antigens (page 10, lines 9-23), wherein the preferred antigens are tumor associated antigens (page 6, lines 12-24) and that useful tumor associated antigens are her2/neu (page 14, lines 16-18). Mizzen et al do not specifically teach the extracellular domain of said protein.

Hudziak et al teach a vaccine comprising the extracellular portion of the HER2 molecule which may be combined with suitable adjuvants (column 2, lines 60-63). Hudziak et al teach that many breast cancer patients exhibit amplification of the her2 gene (column 10, lines 14-16) and said patients would be expected to benefit from active specific immunotherapy by provoking an immune response in a patient with an immunogenic form of the extracellular domain of HER2 (column 10, lines 38-43)

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to use the extracellular domain of HER2 as the tumor-associated antigen in the vaccine taught by Mizzen et al.

One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Hudziak et al on the benefits expected in patients having breast cancer characterized by amplification of Her2, and in addition from the teachings of Mizzen et al on compositions comprising stress proteins and tumor antigens such as Her2.

Claims 1-5, 7-10, 16-23, 34 and 46-57 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for eliciting an anti-tumor immune response against a pre-existing tumor in a subject , does not reasonably provide enablement for a method of prophylactic ally generating an anti-tumor immune response before the tumor occurs. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. Claims 1-5, 7-10 and 16-23 encompass vaccines for inhibiting the growth of a tumor in a subject and for the inhibition of cancer in a subject. when given the broadest reasonable interpretation the inhibition of a tumor in a subject reads on the generation of a prophylactic immune response before the tumor occurs. Claim 34 and dependent claims 46-57 are clearly drawn to the prevention of cancer. The specification is not enabling for the use of the disclosed compositions in the prevention of cancer. This would require administration of the claimed formulations prior to the development of the cancer. However, there is no guidance in the specification for determining the appropriate time prior to the development of malignancy to begin the therapy or for identifying patients at risk for developing malignancy. The specification provides insufficient guidance with regard to the issues raised above and provides no working examples which would provide guidance to one skilled in the art and no evidence has been provided which would allow one of skill in the art to predict the efficacy of the claimed methods with a reasonable expectation of success. In view of the above, one of skill in the art would be forced into undue experimentation to practice the claimed invention.

All other rejections and objections as set forth in the prior Office action are withdrawn in light of applicants arguments and amendments.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Canella whose telephone number is (571) 272-0828. The examiner can normally be reached on Monday through Friday from 9 am to 6:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (571) 272-0871. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Karen A. Canella

Karen A. Canella, Ph.D.
Primary Examiner, Group 1642
01/25/04